

LETTERS

Long-term ACE Inhibitor Therapy in Diabetic Nephropathy: Potential Hazard?

There is now an increasing long-term use of angiotensin-converting enzyme inhibitors (ACEIs) in the management of both incipient¹ and confirmed diabetic nephropathy² due to the established reno-protective effects of this class of drugs. However their side-effect profile has limited their universal usage, with concerns regarding the prevalence of cough (reported to be as high as 20%), first-dose hypotension (particularly with diuretic co-administration), precipitation of acute renal failure in the presence of renal artery stenosis and, on rare occasions, angioedema. Two recent cases of hyperkalaemia in association with ACEI therapy in diabetic nephropathy over several years have highlighted a potentially life-threatening but reversible side-effect of long-term therapy.

The first case is a 64-year-old woman with 8 years of known Type 2 diabetes mellitus (DM) complicated by diabetic retinopathy, nephropathy, and hypertension. Prior to commencement of ACEI therapy, serum potassium was 4.3 mmol L⁻¹. After 6 years of continuous lisinopril (5 mg) treatment, serum potassium was consistently >6.0 mmol L⁻¹ with normal renal function. On ACEI withdrawal, serum potassium returned to pre-treatment level (4.7 mmol L⁻¹) within 2 weeks. The second case of hyperkalaemia occurred in a 75-year-old woman with 14 years of Type 2 DM with confirmed diabetic retinopathy, nephropathy, renal impairment (urea 11.6 mmol L⁻¹, creatinine 156 mmol L⁻¹ before ACEI treatment) and hypertension. After 14 years of ACEI therapy (enalapril 10 mg for 12 years which was replaced by perindopril 2 mg over the last 2 years), serum potassium was 6.0 mmol L⁻¹, urea 22.2 mmol L⁻¹, creatinine 292 mmol L⁻¹. On withdrawal of ACEI, serum potassium fell to 5.6 mmol L⁻¹, urea to 18.9 mmol L⁻¹, and creatinine to 245 mmol L⁻¹.

Both cases developed potentially hazardous hyperkalaemia following long-term ACEI therapy and occurred in the absence of other causes known to induce hyperkalaemia, such as increased potassium ingestion, treatment with potassium-sparing diuretics or non-steroidal anti-inflammatory drugs. The hyperkalaemia in the second case may have been secondary to the deterioration in renal function and compounded by ACEI, as both electrolyte and renal biochemistry improved on drug withdrawal. This suggests the

presence of co-existent renovascular disease. Diabetic patients may be at higher risk of developing hyperkalaemia due to the high prevalence of hyporeninaemic hypoaldosteronism,³ direct effects of hyperglycaemia itself⁴ or the presence of occult renovascular disease.

In a single recent survey in over 1700 diabetic outpatients, hyperkalaemia was found to be relatively common.⁵ With the clear role of ACEI in the long-term management of diabetic nephropathy, therapy should be monitored by serum electrolytes not only before and shortly after initiation, but also as a routine in long-term follow-up.

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Radio Emissions and Accutrend® Malfunction

It has long been recognized that radio waves can induce malfunction of electronic devices. We have recently observed a situation where short-wave radio fields emitted by a radio station may have interfered with the performance of a portable, battery-operated reflectance photometer for determination of blood glucose (Accutrend®, Boehringer, Mannheim).

One of our patients with Type 2 diabetes

mellitus, starting intensified insulin therapy, converted to the use of a glucose meter (Accutrend®) that allowed more rapid measurements than her previously used device (Reflolux S®, Boehringer, Mannheim). She soon realized that at certain times the Accutrend® would produce values that differed substantially from those obtained using the Reflolux S® meter. The deviating Accutrend® results could be erroneously low or high, were not reproducible on a second measurement, and did not correspond to the colour of the test strip. When tested at our clinic, the meter gave satisfactory results both with test solutions and whole blood.

The patient lives only 500 m from a powerful short-wave radio station, which is operated at irregular intervals for international radio transmissions. She questioned whether radio fields emitted by the transmitter might be influencing performance of her meter. To test this hypothesis, she was instructed to compare normal Accutrend® measurements with measurements performed in a large metal box serving as a Faraday cage. On a subsequent occasion, a fasting blood glucose determination produced an unexpectedly low result (1.1 mmol L⁻¹). The patient, who was asymptomatic, performed a second estimation with the meter placed in a metal box. The second determination showed a glucose concentration of 11.3 mmol L⁻¹, in good agreement with a visual reading and a measurement obtained by Reflolux S®.

Boehringer, Mannheim states that the Accutrend® has been tested according to EC regulations and German laws regarding medical devices and their compatibility with electromagnetic fields. This case however suggests that short-wave radio fields may induce malfunction of portable blood glucose meters despite these precautions. In a specific situation individual meters may be affected differently.

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Radio Emissions and Accutrend Malfunction: Reply

Thank you kindly for drawing our attention to this interesting case study. Boehringer Mannheim tests for all conceivable interference possibilities under everyday life circumstances, by complying with the regulations laid down by the EC. Due to the important nature of our devices, Boehringer Mannheim has internally and voluntarily raised these standards even

further, so that compliance to a standard, which reflects use of our instruments in an 'industrial environment' is met.

Based on our precautionary measures and position in the production, development and manufacturing process, we have never experienced any such problems in our internal testing series, nor from users in the market.

For this reason, we are interested in conducting a thorough inspection of the device in question. The exact reasons for the deviating measurements must be ascertained to either validate your interference theory or identify other causes. Generally, it is very important that instructions and warnings as they are laid out in the respective manuals are taken seriously, as they may affect measurements of blood glucose values. This also highlights the importance of appropriate education of patients performing blood glucose self testing. In this case, for instance, it was extremely important that the patient knew how to compare the meter value against the colour coding. We think that it is extremely useful that you are intending to help remind patients with diabetes that one such instruction and warning relates to the possibility of radio wave interference, which generally may affect any type of portable electronic

device, including portable blood glucose meters.

I. Parfremment

Boehringer Mannheim UK Limited, Lewes, East Sussex

Do Radio Emissions Cause Accutrend to Malfunction?

Requirements as to interference immunity—EMI for electronic instruments—have been defined in the European Community since 1994. The compliance with these EMI requirements is documented by the CE-mark. The Accutrend and comparable instruments have a immunity value of 3V/m, which is a requirement defined in the European standard 'EN 50082-1'. The compliance of the Accutrend to that requirement has been validated at Boehringer Mannheim by documented test series. To meet Boehringer Mannheim's heavy demands on quality the Accutrend is designed to meet even the considerably higher immunity requirements of the 'EN 50082-2' standard, which is to be used in an 'industrial' environment.

Even with 10V/m of field strength no malfunction or wrong measurement readings occur. This was proved several

times by test series. In further tests it was shown that the Accutrend even works under far more extreme environmental EMI conditions close to conditions by short-wave-transmitters.¹ To sum up, we have not observed influences to the measurement values of the Accutrend caused by radio emissions in the cases noted above (assuming the Accutrend is in good working condition).

To take the exceptional responsibility towards our customers into account, Boehringer Mannheim points out a tolerable remaining risk in the instructions for use, because theoretically there might be higher field strength, especially when safety distances are not kept. The general restriction to the use of laptops in airplanes is comparable to this kind of situation. This similar situation makes it clear why the instructions for use point out the remaining risks.

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